Remarks

Prior to this amendment, claims 1-31, 33-41, 43-46, 49-59, and 61-64 were pending in this application. Claim 1 is canceled. Claims 2, 25, 28, 31, 49, 58, and 59 are amended herein.

Claim 2 is amended to be in independent form. Claims 25, 28, 49, 58, and 59 are amended to correct dependency. Support for the amendment of claim 31 can be found in the specification at least at page 2, line 10.

Applicants expressly reserve the right to pursue protection of any or all subject matter removed by the current amendment in a subsequent application. No new matter has been added by these amendments. After entry of this amendment, claims 2-31, 33-41, 43-46, 49-59, and 61-64 are pending in this application.

Telephone Interview

Applicants thank Examiner Nguyen for the courtesy of the telephone interview with their representative, Dr. Anne Carlson, on February 21, 2007. During the interview, the restriction requirement was discussed.

Restriction Requirement

Claims 1-31, 33-41, 43-46, 49-59, and 61-64 of this §371 National Stage application were indicated as being subject to a restriction requirement (finding of lack of unity). In particular, the following Groups have been designated:

Group I.	Claims 1-4, 14, 22-24, and 58 drawn to a substantially purified RFX4_v3 polypeptide and a method for screening compounds for the ability to alter RFX4_v3 activity using the same;
Group II.	Claims 5-13, 15-21 and 25-27 drawn to an isolated nucleic acid molecule encoding a RFX4_v3 polypeptide, a vector, or host cell comprising the same an a method for producing a variant of the same;
Group III.	Claims 28-30 drawn to a method for detecting a nucleic acid molecule in a biological sample;
Group IV.	Claims 31, 33-35, 40-41, and 44-45 drawn to a method for identifying a subject at risk of developing RFX4_v3 linked hydrocephalus by detecting in the subject a mutation in a RFX4_v3 nucleotide sequence, and a kit comprising a nucleic acid probe that specifically detects a mutation in a RFX4_v3 allele;
Group V.	Claims 31, 36-41 and 43 drawn to a method for identifying a subject at risk of developing RFX4_v3 linked hydrocephalus by detecting in the subject a mutation in a RFX4_v3 polypeptide;

Group VI. Claims 44 and 46 drawn to a kit comprising an antibody that specifically binds and detects a mutation in the protein expressed by a mutated RFX4_v3 allele;

Group VII. Claim 49 drawn to an antibody that specifically binds to a substantially purified RFX4_v3 polypeptide;

Group VIII. Claims 50-57 drawn to a method for generating a non-human transgenic animal with a knockout for the RFX4_v3 gene, and a transgenic mouse whose somatic and germ cells comprise a disrupted endogenous RFX4_v3 gene;

Group IX. Claims 59 and 61-62 drawn to a pharmaceutical composition comprising a therapeutically effective amount of RFX4_v3 polypeptide, variant or portion thereof and a pharmaceutically acceptable carrier, and a method of treating congenital hydrocephalus in a subject using the same;

Group X. Claims 59, 61 and 63-64 drawn to a pharmaceutical composition comprising a therapeutically effective amount of a nucleic acid sequence encoding a RFX4_v3 polypeptide, variant or portion thereof and a pharmaceutically acceptable carrier, and a method of treating congenital hydrocephalus in a subject using the same.

The Office action states that the inventions of Groups I-X do not relate to a single general inventive concept under PCT Rule 13.1 because the compositions of Groups I, II, VI, VII, VIII, IX, and X "are compositions that are different chemically one from the others" (Office action at page 3) and the "methods in Groups I-V and VIII-X are different one from the others" because "[e]ach different method step can be considered to be a special technical feature"; and therefore the methods listed in Groups I-V, VIII-X lack the same or corresponding special technical feature" (Office action at page 3). In light of the above comments, Applicants submit that the claims have been incorrectly restricted into Groups using the rules related to U.S. restriction practice, rather than applying the lack of unity standards under PCT Rule 13.1. All of the Groups do in fact relate to a single special technical feature, which feature makes a contribution over the prior art. As such, all of the claims should be examined together. Applicants request that the requirement be withdrawn in light of the arguments and amendments herein.

Standard for Analyzing Unity of Invention

37 CFR § 1.475 requires unity of invention in a National Stage application such as this; unity of invention is present when a group of inventions are "so linked as to form a single general inventive concept." [*See* 37 CFR § 1.475(a).] "A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature." [MPEP § 1893.03(d). *See also* 37 CFR § 1.475(a).]

Further, "The expression 'special technical features' shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art." [*See* 37 CFR § 1.475(a), emphasis added.]

This makes it clear that an analysis with regard to unity of invention occurs in two stages. First, is there a special technical feature shared among the claims/groups of inventions, such that they are linked to form a single inventive concept? If there is, then one asks does that special technical feature **define a contribution over the prior art** for each of the claimed inventions? If no relevant prior art is identified, then there can be no finding of lack of unity.

Applying the Standard in the Current Case

Groups I through X are linked to form a single general inventive concept. Claim 1 is canceled and claim 2 is amended to be in independent form. Upon a review of the application and the claims, it is clear that the invention as claimed relates to the substantially purified RFX4_v3 polypeptide of amended claim 2, wherein the polypeptide comprises:

a) an amino acid sequence at least 70% identical to an amino acid sequence set forth as SEQ ID NO: 8;

b) a conservative variant of the amino acid sequence set forth as SEQ ID NO:8; or

c) the amino acid sequence set forth as SEQ ID NO: 8,

wherein the polypeptide has RFX4_v3 activity, and the N-terminus of the polypeptide is at least 90% identical to residues 1-14 of SEQ ID NO: 8.

Claims 2-31, 33-41, 43-46, 49-59, and 61-64 (Groups I-X) either depend from amended claim 2 (thereby incorporating all of the limitations thereof) or are linked by the special technical feature of the substantially purified RFX4_v3 polypeptide. Thus, claims 2-31, 33-41, 43-46, 49-59, and 61-64 all relate to the special technical feature of the substantially purified RFX4_v3 polypeptide.

Moreover, this special technical feature does define a contribution over the prior art for each Group of inventions. There is no reference of record in the case that reads on the substantially purified RFX4_v3 polypeptide of original claim 1 or claim 2; the International Search Report dated August 23, 2005, failed to identify a prior art reference of particular relevance and the International Preliminary Examination Report (IPER) dated October 26, 2005, specifically states that claims 1 and 2 "meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly

suggest the presently claimed invention" (IPER, Section V). In addition, no reference has been cited in the current Restriction Requirement, which would appear to be a clear admission that there is no relevant prior art. Thus, this special technical feature does define a contribution over the prior art for each Group of inventions. This feature is a basis for patentability of Applicants' invention.

As **required by 37 CFR § 1.475**, the claims of Groups I-X have unity of invention because they are directed "to a group of inventions so linked as to form a single general inventive concept" because "there is a technical relationship among [the] inventions involving one . . . corresponding technical feature[]" – a substantially purified RFX4_v3 polypeptide – and this special technical feature "define[s] a contribution . . . over the prior art."

As unity of invention exists among Groups I-X in the present application, it is inappropriate to subject claims 2-31, 33-41, 43-46, 49-59, and 61-64 to a requirement for restriction. Applicants request that the requirement be withdrawn, that Groups I-X be rejoined, and that the corresponding claims be examined in the current case. In the event that Groups I-X are not rejoined, Applicants expressly request that the restriction of the claims in this §371 National Stage case be re-evaluated, as required, under the lack of unity standards of PCT Rule 13.1 and that *a new restriction requirement be issued.*

Election

Applicants note that the International Search Report (ISR), dated August 23, 2005, for this application, alleging a lack of unity of invention, divided the claims into eight different Groups, instead of the ten Groups identified in the current Restriction Requirement. A copy of the ISR is attached as Exhibit A. Under protest, and only to comply with 37 CFR §1.499, Applicants hereby provisionally elect Examiner's Group III *as set forth in the ISR* (corresponding to claims 15-21, 26-35, 40-41, and 44-45). Claims 15-21 of Group III are directed to an isolated nucleic acid molecule that hybridizes to the recited target nucleic acid molecule, a vector, and a transformed host cell. Similarly, the claims of Group II *as set forth in the ISR* (claims 4-13 and 25) are directed to a nucleic acid molecule encoding RFX4_v3 polypeptide, a vector, a transformed host cell, as well as a method for producing a variant of a RFX4_v3 polypeptide by mutagenizing the wild-type sequences. As there is no undue burden to search the claims of Groups II and III together, Applicants respectfully request that the Examiner reconsider the lack of unity with regard to ISR Groups II and III, and rejoin these Groups.

If the Examiner will not consider rejoining Groups II and III of the ISR, Applicants hereby provisionally elect Examiner's Group II of the Restriction Requirement (corresponding to claims 5-13, 15-21, and 25-27, drawn to an isolated nucleic acid molecule encoding a RFX4_v3 polypeptide, a vector, or host cell comprising the same an a method for producing a variant of the same). Applicants expressly request that the claims of Group IV of the Restriction Requirement, which depend from or otherwise include all the limitations of claims directed to an isolated nucleic acid molecule encoding a substantially purified RFX4_v3 polypeptide, be rejoined and the claims examined, at the latest upon the allowance of any of the product claims. It is believed that this is in accordance with the current Patent and Trademark Office Guidelines for Restriction Requirements in TC1600.

In accord with 37 CFR §1.143, Applicants specifically reserve the right to petition to have the appropriateness of the finding of lack of unity/restriction requirement reconsidered, if it is maintained in spite of this response.

Conclusion

It is believed that the application is in condition for substantive examination. If any minor matters remain to be addressed prior to examination, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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